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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/856,694	08/13/2001	Jan C. Simon	24741-1525	1918

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EXAMINER	
DAVIS, RUTH A	
ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 11/05/2002 16

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/856,694	SIMON ET AL.	
	Examiner	Art Unit	
	Ruth A. Davis	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 August 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *36-54,56* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *36-54 and 56* is/are rejected.

7)☒ Claim(s) *36,38,43* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Applicant's amendment has been received and entered into the case. Claim 55 has been cancelled. Claims 36 – 54 and 56 are pending and have been considered on the merits. All arguments have been fully considered.

Claim Objections

1. Claims 36, 38 and 43 are objected to because of the following informalities:

In claim 36, line 5, ":" should be deleted; in claim 38 line 2, ":" should be deleted; in claim 43, line 1, "." should be deleted. Appropriate correction is required.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 36 – 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over The Hypericum Home Page (1996) in view of The Merck Manual.

Applicant claims a method for treating a condition selected from cancer, inflammatory skin diseases, precancerous conditions, geriatric skin or microbial skin infections comprising topical administration of an effective amount of a composition consisting of (a) pharmaceutically acceptable carrier and (b) an active agent consisting of (i) hyperforin or (ii) hyperforin and hypericin, to a subject in need thereof. Specifically, the condition is eczema, or is selected from exsiccation eczemas, hyperkeratotic hand/foot eczemas, contact eczemas, atopic dermatitis, neurodermatitis, lichen simplex, prurigo simplex, lymphoma, leukemia, melanoma, epithelial precancerous conditions, tumor metastases or epithelial tumors. The subject is a mammal and the composition is a topical ointment with an effective amount of at least 15 micrograms hyperforin per ml, 0.02 – 20 mg/ml, 1 – 20 mg/ml or 10 mg/ml; or 15 micrograms/ml or 20 – 150 micrograms/ml hypericin.

The Hypericum Home Page (HHP) teaches extracts of Hypericum perforatum (St. John's Wort) include hypericin and hyperforin wherein the extracts exhibit anti-inflammatory and antibacterial effects when externally, or topically, applied (p.3). HHP specifically teaches that hyperforin is attributed with anti-inflammatory and antibacterial effects (p.3).

HHP does not teach a method for treating an inflammatory condition with the claimed effective amounts or the claimed specified conditions. However at the time of the claimed invention, it would have been obvious to one of ordinary skill in the art to use hyperforin and/or hyperforin and hypericin in a method for treating inflammatory conditions because of the disclosed anti-inflammatory effect. Further, at the time of the claimed invention, it would have been obvious to one of ordinary skill in the art to optimize effective volumes and concentrations as a matter of routine experimentation. Still further, it would have been obvious to one of ordinary skill in the art to include a pharmaceutical carrier because it was routine practice in the art at the time the claimed invention was made. Moreover, at the time of the invention, one of ordinary skill in the art would have been motivated to use hyperforin in a method for treating anti-inflammatory conditions with a reasonable expectation of success because of its known benefit as disclosed by HHP.

HHP does not specifically teach the extracts are effective against eczema, or the other conditions as claimed. However, at the time of the claimed invention, it was well known in the art that eczemas are characterized by inflammation (See "The Merck Manual", cited on PTO-892). Specifically, eczema, contact eczema, atopic eczema, hand and foot eczemas, and lichen simplex are each characterized as superficial inflammations of the skin of varying degrees. In further support, Shroot et al. teaches inflammatory diseases include dermatitis and eczema (col.1 line 12-15) and Lacefield teaches inflammatory conditions include atopic dermatitis, contact dermatitis, eczema, lichen simplex and chronic dermatoses. At the time of the invention, it would have been obvious to one of ordinary skill in the art to treat any of the aforementioned eczemas with hyperforin because of the anti-inflammatory effect as disclosed by HHP.

Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by HHP and Merck to utilize hyperforin in a method for treating inflammation and eczemas with a reasonable expectation for success.

Applicant argues that the HHP and Merck references do not have publication dates prior to the effective filing date of the claimed invention and that the dates have not been sufficiently established prior to the print out dates of the references. Applicant additionally argues that while the references teach hyperforin/hypericin treats inflammatory conditions, bacterial infections and cancers, they do not teach the specific conditions or amounts as claimed. Finally applicant argues that there is no motivation, suggestion, or expectations of success from the references to obtain the claimed compositions.

However, these arguments fail to persuade because the HHP reference shows a copyright date of 1996, which is before the earliest priority date (11/25/1998) of the claimed invention. 35 USC 102 states conditions for patentability, novelty and loss of right to patent: A person shall be entitled to a patent unless (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent; (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States. MPEP section 2132 states that "Known or Used" Means Publicly Known or Used. "The statutory language known or used by others in this country' (35 U.S.C. § 102(a)), means knowledge or use which is accessible to the public." Carella v. Starlight Archery, 804 F.2d 135, 231 USPQ 644 (Fed. Cir. 1986). The

knowledge or use is accessible to the public if there has been no deliberate attempt to keep it secret. W. L. Gore & Assoc. v. Garlock, Inc., 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983). In addition, a prima facie case is made out under 35 U.S.C. 102(a) if, within 1 year of the filing date, the invention, or an obvious variant thereof, is described in a "printed publication" whose authorship differs in any way from the inventive entity unless it is stated within the publication itself that the publication is describing the applicant's work. In re Katz, 687 F.2d 450, 215 USPQ 14 (CCPA 1982). MPEP section 2128 – 2128.02 states that a reference is a printed publication if it is accessible to the public. A reference is proven to be a "printed publication" "upon a satisfactory showing that such document has been disseminated or otherwise made available to the extent that persons interested and ordinarily skilled in the subject matter or art, exercising reasonable diligence, can locate it." In re Wyer, 655 F.2d 221, 210 USPQ 790 (CCPA 1981) (quoting I.C.E. Corp. v. Armco Steel Corp., 250 F. Supp. 738, 743, 148 USPQ 537, 540 (SDNY 1966)) ("We agree that printed publication' should be approached as a unitary concept. The traditional dichotomy between printed' and publication' is no longer valid. Given the state of technology in document duplication, data storage, and data retrieval systems, the probability of dissemination' of an item very often has little to do with whether or not it is printed' in the sense of that word when it was introduced into the patent statutes in 1836. In any event, interpretation of the words printed' and publication' to mean probability of dissemination' and public accessibility' respectively, now seems to render their use in the phrase printed publication' somewhat redundant.") In re Wyer, 655 F.2d at 226, 210 USPQ at 794.

Further, an electronic publication, including an on-line database or Internet publication, is considered to be a "printed publication" within the meaning of 35 U.S.C. 102(a) and (b) provided

the publication was accessible to persons concerned with the art to which the document relates. See In re Wyer, 655 F.2d 221, 227, 210 USPQ 790, 795 (CCPA 1981); Amazon.com v. Barnesandnoble.com, 73 F. Supp. 2d 1228, 53 USPQ2d 1115, 1119 (W.D. Wash. 1999; and In re Epstein, 32 F.3d 1559, 31 USPQ2d 1817 (Fed. Cir. 1994).

In the instant case, the HHP reference relied on clearly has a copyright date of 1996, thus the reference was accessible to the public, there was no deliberate attempt to keep it secret and the document has been disseminated or otherwise made available to the extent that persons interested and ordinarily skilled in the subject matter or art, exercising reasonable diligence, can locate it. As such, the reference would appear to qualify as prior art under 35 USC 102 (a) and (b).

The Merck Manual is relied upon to demonstrate the state of the art in that the claimed conditions are, by definition, inflammatory conditions. Since such characteristics are intrinsic properties of the claimed conditions, one of ordinary skill in the art would have been motivated by HHP to treat any of the named inflammatory disorders with a reasonable expectation of successfully treating the inflammatory disorders.

Although the references do not teach the claimed amounts or conditions, it would have been well within the purview of one of ordinary skill in the art to determine effective amounts as well as the variety of inflammatory conditions for which known the anti-inflammatory agent hyperforin is effective, as a matter of routine experimentation. Therefore, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by HHP to treat inflammatory skin conditions with hyperforin and/or hyperforin and hypericin with a reasonable expectation of success.

4. Claims 36, 38 – 43, 46 – 49 and 56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Valavichyus (1986).

Applicant claims a method for treating a condition selected from cancer, inflammatory skin diseases, precancerous conditions, geriatric skin or microbial skin infections comprising topical administration of an effective amount of a composition consisting of (a) pharmaceutically acceptable carrier and (b) an active agent consisting of (i) hyperforin or (ii) hyperforin and hypericin, to a subject in need thereof. The condition is selected from exsiccation eczema, hyperkeratotic hand and foot eczema, contact eczema, atopic dermatitis, neurodermatitis, lichen simplex, prurigo simplex, lymphoma, leukemia, melanoma, epithelial precancerous conditions, tumor metastases or epithelial tumor. The subject is a mammal. Applicant additionally claims a method of treating cancer comprising administering to a subject in need thereof an effective amount of a composition comprising hyperforin and a pharmaceutically acceptable carrier. The effective amount comprises at least 50 micrograms hyperforin/ml in an injectable form, 100 micrograms/microliter suitable for epicutaneous application, 50 micrograms/ml for systemic administration. The hyperforin is at least 90% pure.

Valavichyus teaches extracts of St. John's Wort, specifically oil extracts, inhibits growth of sarcoma (cancer) cells (abstract). Valavichyus also teaches that administration of the extracts inhibited growth of tumors in animals (or subjects in need thereof). At the time the claimed invention was made, it was known in the art that oil preparations of St. John's Wort are hypericin

free and contain high concentrations of hyperforin (See Chavez, p.1622). It was also known in the art that plant oils were used as pharmaceutical carriers.

Valavichyus does not teach the method wherein the claimed volumes and concentrations were used, modes of administration, or wherein the hyperforin is at least 90% pure. However, at the time of the claimed invention, it would have been well within the purview of one of ordinary skill in the art to optimize effective volumes, modes of administration and purity of effective agents as a matter of routine experimentation. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by routine practice to optimize the effective amounts of Valavichyus with a reasonable expectation for successfully treating cancer.

Applicant argues that Valavichyus uses a combination of St. John's and chamomile making it unclear which agent is the effective agent and that the effective volumes and concentrations of hyperforin are not disclosed. Applicant additionally argues that there is not motivation or suggestion in the references to use the claimed amounts of hyperforin and/or hypericin.

However, these arguments fail to persuade because Valavichyus specifically teaches oil extracts of St. John's wort is effective for inhibiting sarcoma cells. The reference specifically teaches administering a composition comprising an oil extract of St. John's Wort (containing hyperforin) for treating cancer, as instantly claimed. Furthermore, although the reference does not teach the claimed effective concentrations, as discussed above, it would have been obvious to one of ordinary skill in the art to optimize such effective amounts as it was routinely practice in the art at the time claimed invention was made. Therefore, at the time of the claimed invention,

one of ordinary skill in the art would have been motivated by Valavichyus to treat cancer with oil extracts of St. John's wort (or hyperforin) with a reasonable expectation of success.

5. Claims 36, 38 – 54 and 56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Valavichyus in view of HHP and/or DeCosterd.

Applicant claims a method for treating a condition selected from cancer, inflammatory skin diseases, precancerous conditions, geriatric skin or microbial skin infections comprising topical administration of an effective amount of a composition consisting of (a) pharmaceutically acceptable carrier and (b) an active agent consisting of (i) hyperforin or (ii) hyperforin and hypericin, to a subject in need thereof. Specifically, the condition is selected from exsiccation eczema, hyperkeratotic hand and foot eczema, contact eczema, atopic dermatitis, neurodermatitis, lichen simplex, prurigo simplex, lymphoma, leukemia, melanoma, epithelial precancerous conditions, tumor metastases or epithelial tumor. The subject is a mammal, and the composition is a topical ointment and the effective amount is at least 15 micrograms hyperforin per ml, 0.02 – 20 mg/ml, 1 – 20 mg/ml, 10 mg/ml, at least 15 micrograms hypericin/ml or 20 – 150 micrograms hypericin/ml. Applicant additionally claims a method of treating cancer comprising administering to a subject in need thereof an effective amount of a composition comprising hyperforin and a pharmaceutically acceptable carrier. The effective amount comprises at least 50 micrograms hyperforin/ml in an injectable form, 100 micrograms/microliter suitable for epicutaneous application, 50 micrograms/ml for systemic administration. The cancer

is melanoma, lymphoma, skin cancer, mammary carcinoma or leukemia carcinoma and the hyperforin is at least 90% pure.

Valavichyus teaches extracts of St. John's Wort, specifically oil extracts, inhibits growth of sarcoma (cancer) cells (abstract). Valavichyus also teaches that administration of the extracts inhibited growth of tumors in animals (or subjects in need thereof). At the time the claimed invention was made, it was known in the art that oil preparations of St. John's Wort are hypericin free and contain high concentrations of hyperforin (See Chavez, p.1622). It was also known in the art that plant oils were used as pharmaceutical carriers.

The Valavichyus does not teach the method with the claimed volumes/concentrations, modes of administration, or wherein the hyperforin is at least 90% pure. However, at the time of the claimed invention, it would have been well within the purview of one of ordinary skill in the art to optimize effective volumes, modes of administration and purity of effective agents as a matter of routine experimentation. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by Valavichyus and routine practice to optimize the effective amounts of hyperforin with a reasonable expectation for successfully treating cancer.

Valavichyus does not teach the method wherein the cancer is melanoma, lymphoma, skin cancer, mammary carcinoma and leukemia carcinoma. However, HHP teaches extracts of Hypericum perforatum (St. John's Wort) include hypericin and hyperforin wherein the extracts demonstrate anticancer properties and have been proven to inhibit tumor cells of the brain, lung and skin (p.4). In addition, DeCosterd teaches extracts of Hypericum inhibit growth of colon carcinomas (abstract). Specifically, DeCosterd teaches derivatives of hyperforin exhibit the

growth-inhibiting activity (abstract). As evidenced by the cited references, at the time of the invention, hyperforin, derivatives thereof and extracts of Hypericum were well known as effective agents against cancers of various kinds. Although the supporting references do not specifically teach the agents in methods for treating a subject in need thereof, they do suggest that such activity would be expected. Therefore, one of ordinary skill in the art would have been motivated to use the extracts in treating cancers (i.e. lymphoma, mammary and leukemia carcinomas) because of the demonstrated effectiveness in a variety of cancers as disclosed by the references above. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by Valavichyus, HHP and DeCosterd to use compositions comprising hyperforin or hyperforin and hypericin in the methods for treating various cancers with a reasonable expectation of success.

Applicant argues that Valavichyus uses a combination of St. John's and chamomile making it unclear which agent is the effective agent and that the effective volumes and concentrations of hyperforin are not disclosed. Applicant additionally argues that there is not motivation or suggestion in the references to use the claimed amounts of hyperforin and/or hypericin.

However, these arguments fail to persuade because Valavichyus specifically teaches oil extracts of St. John's wort is effective for inhibiting sarcoma cells. The reference specifically teaches administering a composition comprising an oil extract of St. John's Wort (containing hyperforin) for treating cancer, as instantly claimed. Furthermore, although the reference does not teach the claimed effective concentrations, as discussed above, it would have been obvious to

one of ordinary skill in the art to optimize such effective amounts as it was routinely practice in the art at the time claimed invention was made. Therefore, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by Valavichyus to treat cancer with oil extracts of St. John's wort (or hyperforin) with a reasonable expectation of success.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruth A. Davis whose telephone number is 703-308-6310. The examiner can normally be reached on M-H (7:00-4:30); altn. F (7:00-3:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 703-308-4743. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Ruth A. Davis; rad
October 31, 2002

LEON B. LANKFORD, JR.
PRIMARY EXAMINER